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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re reissue application of: U.S. Pat. No. 6,348,481, issued February 19, 2002

Applicants: Yoshiyuki INADA, et al.

Title: PHARMACEUTICAL COMPOSITION FOR ANGIOTENSIN II-MEDIATED DISEASES

Appl. No.: 10/781,263

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Art Unit: 1626

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SUBSTITUTE BROADENING REISSUE DECLARATION UNDER 37 CFR § 1.175

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, Yoshiyuki Inada and Keiji Kubo, hereby declare that:

1. My residence, post office address, and citizenship are stated below next to my name.

2. I understand the written English language at least well enough to understand the content of present declaration and the content of any document(s) to which the present declaration relates.

3. I believe that the inventors listed below are the original, joint, and first inventors of the subject matter described and claimed in our U.S. Patent 6,348,481 and in the foregoing specification for which a reissue patent is sought on the invention entitled "PHARMACEUTICAL COMPOSITION FOR ANGIOTENSIN-II MEDIATED DISEASES."

4. U.S. Patent No. 6,348,481 claims priority to the following U.S. patent applications and foreign patent applications:

This Application is a Divisional of 09/563,855 filed 05/04/2000, which is a Continuation of 09/287,167, filed 04/06/1999, which is a Continuation of 08/883,040, filed 06/26/1997, which is a Divisional of 08/351,011, filed 12/07/1994, which is a Continuation-in-part of 08/254,541, filed 06/06/1994, which claims priority to JP 135524-1993, filed 06/07/1993.

5. I believe that originally issued United States Letters Patent No. 6,348,481 ("'481 patent") may be partly inoperative or invalid by reason of the Petitioner claiming more or less than Petitioner had the right to claim in the patent and for the reason that Petitioner failed to provide claims directed to a subgenus of the originally disclosed invention. The error in failing to provide claims directed to a subgenus which comprises one of the three recited species in combination with a compound having diuretic activity or a compound having calcium antagonist activity was discovered as a result of discussions involving Petitioner's attorneys. During these discussions, it was discovered that claims directed to this subgeneric invention were lacking in the scope of coverage. It was error for Petitioner to omit a set of claims directed to this subgenus which comprises one of the three recited species in combination with a compound having diuretic activity or a compound having calcium antagonist activity.

Claims 4-10 were added in a preliminary amendment filed February 19, 2004 to correct this deficiency. Claim 4 is directed to a pharmaceutical composition which comprises at least one of (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7 -carboxylate, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7- carboxylic acid, or 2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methy l]-1H-benzimidazole-7-carboxylic acid or a pharmaceutically acceptable salt in combination with a compound having diuretic activity or a compound having calcium antagonistic activity.

The species, (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7 –carboxylate, is recited in the specification at column 15, lines 24-26, column 17, lines 40-42 and lines 55-57, column, 19, lines 5-7 and lines 21-23, column 20, lines 54-57, column 21, lines 5-8 and lines 59-62 and column 22, lines 16-19.

The species, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7- carboxylic acid, is recited in the specification at column 16, lines 57-58, column 17, lines 5-7, as the disodium salt at column 18, lines 6-8, column, 19, lines 60-62, column 20, lines 18-20 and lines 35-37 and column 21, lines 25-27 and lines 40-42.

The species, 2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methy l]-1H-benzimidazole-7-carboxylic acid, is recited in the specification at column 19, lines 41-43 and lines 60-62.

The genus of compounds having diuretic activity is recited in the specification at column 10, lines 29-42. The genus of compounds having calcium antagonistic activity is recited in the specification at column 10, lines 43-50.

Claim 5 is dependent upon claim 4 and recites a Markush group of substances known to have diuretic activity. This list is recited in the specification at column 10, lines 29-42.

Claim 6 is dependent upon claim 4 and recites a Markush group of substances known to have calcium antagonistic activity. This list is recited in the specification at column 10, lines 43-50.

Claim 7 is a method of use claim which is directed to a method for the treatment of angiotensin II mediated diseases in a mammal in need thereof which comprises administering an effective amount at least one of (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7 -carboxylate, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7- carboxylic acid, or 2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methy l]-1H-benzimidazole-7-carboxylic acid or a pharmaceutically acceptable salt in combination with a compound having

diuretic activity or a compound having calcium antagonistic activity. The species, (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7 –carboxylate, is recited in the specification at column 15, lines 24-26, column 17, lines 40-42 and lines 55-57, column, 19, lines 5-7 and lines 21-23, column 20, lines 54-57, column 21, lines 5-8 and lines 59-62 and column 22, lines 16-19.

The species, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7- carboxylic acid, is recited in the specification at column 16, lines 57-58, column 17, lines 5-7, as the disodium salt at column 18, lines 6-8, column, 19, lines 60-62, column 20, lines 18-20 and lines 35-37 and column 21, lines 25-27 and lines 40-42.

The species, 2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methy l]-1H-benzimidazole-7-carboxylic acid, is recited in the specification at column 19, lines 41-43 and lines 60-62.

The genus of compounds having diuretic activity is recited in the specification at column 10, lines 29-42. The genus of compounds having calcium antagonistic activity is recited in the specification at column 10, lines 43-50.

Claim 8 is dependent upon claim 7 and recites specific angiotensin II mediated diseases. The angiotensin II mediated disease are recited in the specification at column 10, lines 51-61.

Claim 9 is dependent upon claim 7 and recites a Markush group of substances known to have diuretic activity. This list is recited in the specification at column 10, lines 29-42.

Claim 10 is dependent upon claim 7 and recites a Markush group of substances known to have calcium antagonistic activity. This list is recited in the specification at column 10, lines 43-50.

Therefore, Petitioner submits that the claims 4-10 added in the Preliminary Amendment filed February 19, 2004 provide a subgenus relative to the originally issued claims. In view of these claims, Petitioner believes that this reissue application provides

claims directed to a subgenus of the originally filed claims which correct the failure to claim the subgeneric invention invented by Yoshiyuki Inada and Keiji Kubo. All errors which are being corrected in the present reissue application up to the time of filing of this declaration arose without any deceptive intent on Petitioner's part.

6. By this reissue declaration, we desire to seek broadened claims, and, this application for reissue of the original Letters Patent addresses the aforementioned errors in claiming less than we were entitled to claim by including claims 4-10.

7. I believe the inventors named below to be the original and first inventors of the subject matter which is claimed and for which a patent is sought on the invention in the present application no. 10/781,263, entitled:
PHARMACEUTICAL COMPOSITION FOR ANGIOTENSIN II-MEDIATED DISEASES
the amended claims of which are as follows:

1. A method for the treatment of angiotension II-mediated disease in a mammal in need thereof which comprises administering an effective amount of
(±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate,
2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or
2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or a pharmaceutically acceptable salt thereof, in combination with an effective amount of furosemide.

2. A method according to claim 1, wherein the disease is hypertension, cardiac insufficiency, ischemic peripheral circulation disturbances, myocardial ischemia, vein insufficiency, progressive cardiac insufficiency after myocardial infarction, diabetic nephritides, nephritis, arteriosclerosis, hyperaldosteronism, dermatosclerosis, glomerulosclerosis, renal insufficiency, diseases of central nervous system, sensory disturbances,

deficiency of memory, depression, amnesia and senile dementia, anxiety neurosis, catatonia, glaucoma, or intraocular high tension.

3. A method according to claim 1, wherein the disease is hypertension.

4. A pharmaceutical composition which comprises at least one of : (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or 2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or a pharmaceutically acceptable salt thereof, in combination with a compound having diuretic activity or a compound having calcium antagonistic activity.

5. The composition of claim 4, in which the compound having diuretic activity is a member selected from the group consisting of amiloride, chlorothiazide, benzthiazide, ticrynafen, acetazolamide, aminophylline, cyclothiazide, cyclopenthiazide, methyclothiazide, benzylhydrochlorothiazide, penfluthiazide, ethiazide, hydroflumethiazide, polythiazide, clofenamide, chlorthalidone, cyclothiazide, bendroflumethiazide, meticrane, tripamide, metolazone, quinethazone, bumetanide, mefruside, azosemide, ethacrynic acid, sodium ethacrynate, piretanide, spironolactone, potassium canrenoate and triamterene.

6. The composition of claim 4, in which the compound having calcium antagonistic activity is a member selected from the group consisting of diltiazem hydrochloride, terolidine hydrochloride, nicardipine hydrochloride, barnidipine hydrochloride, flunarizine hydrochloride, verapamil hydrochloride, cinnarizine, nisoldipine, nitrendipine, nifedipine, nilvadipine, felodipine, nildipine, nimodipine, penidipine and benidipine.

7. A method for treatment of angiotensin II mediated diseases in a mammal in need thereof which comprises administering an effective amount of at least one of

(±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate,

2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or

2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or a pharmaceutically acceptable salt thereof, in combination with a compound having diuretic activity or a compound having calcium antagonistic activity.

8. The method of claim 7, in which the angiotensin II-mediated diseases is selected from the group consisting of hypertension, cardiac insufficiency, ischemic peripheral circulation disturbances, myocardial ischemia, vein insufficiency, progressive cardiac insufficiency after myocardial infarction, diabetic nephritides, nephritis, arteriosclerosis, hyperaldosteronism, dermatosclerosis, glomerulosclerosis, renal insufficiency, diseases of central nervous system, sensory disturbances, deficiency of memory, depression, amnesia and senile dementia, anxiety neurosis, catatonia, glaucoma and intraocular high tension.

9. The method of claim 7, wherein the compound having diuretic activity is a member selected from the group consisting of amiloride, chlorothiazide, benzthiazide, ticrynafen, acetazolamide, aminophylline, cyclothiazide, trichloromethiazide, cyclopenthiazide, hydrochlorothiazide, methyclothiazide, benzylhydrochlorothiazide, penfluthiazide, ethiazide, hydroflumethiazide, polythiazide, clofenamide, chlorthalidone, cyclothiazide, bendroflumethiazide, meticrane, tripamide, metolazone, indapamide, quinethazone, furosemide, bumetanide, mefruside, azosemide, ethacrynic acid, sodium ethacrynate, piretanide, spironolactone, potassium canrenoate and triamterene.

10. The method of claim 7, wherein the compound having calcium antagonistic activity is a member selected from the group consisting of diltiazem hydrochloride, terolidine hydrochloride, nicardipine hydrochloride, barnidipine hydrochloride, flunarizine hydrochloride, verapamil hydrochloride, manidipine hydrochloride, cinnarizine, nisoldipine, nitrendipine, nifedipine, nilvadipine, felodipine, nildipine, nimodipine, penidipine and benidipine.

8. I hereby state that I have reviewed and understand the contents of the above-identified specification (attached herewith), including the claims of the preliminary amendment filed February 19, 2004, and the claims as shown in amended form in section 7 above.

9. I have been told that the specification of the application has been amended as follows (brackets indicate **[deleted]** text and underlining indicates **new** text with respect to the original patent, which is attached to this declaration):

THE PARAGRAPH AT COLUMN 10, LINES 29-42 WAS AMENDED AS FOLLOWS:

As compounds having diuretic activity, while mention is made of amiloride, chlorothiazide, hydrochloride, benzthiazide, ticrynafen, acetazolamide, aminophylline, cyclothiazide, trichloromethiazide, cyclopenthiazide, hydrochlorothiazide, methyclothiazide, benzylhydrochlorothiazide, penfluthiazide, ethiazide, hydroflumethiazide, polythiazide, clofenamide, chlorthalidone, cyclothiazide, bendroflumethiazide, meticrane, tripamide, **[methrazone]** **metolazone**, indapamide, quinethazone, furosemide, bumetanide, mefruside, azosemide, ethacrynic acid, sodium ethacrynate, piretanide, spironolactone, potassium canrenoate and triamterene, mention is also made of a mixture of them or a combination of them.

THE PARAGRAPH AT COLUMN 10, LINES 43-50 WAS AMENDED AS FOLLOWS:

As compounds having calcium antagonistic activity, while mention is made of diltiazem hydrochloride, [terodiline] **terolidine** hydrochloride, nicardipine hydrochloride, [valnidipine] **barnidipine** hydrochloride, [flunariziim] **flunarizine** hydrochloride, [varapamyl] **verapamil** hydrochloride, manidipine hydrochloride, cinnarizine, nisoldipine, nitrendipine, nifedipine, nilvadipine, felodipine, nildipine, nimodipine, penidipine and-benidipine; mention is also made of a mixture of them or a combination of them.

THE PARAGRAPH AT COLUMN 14, LINES 8-30 WAS AMENDED AS FOLLOWS:

For example, a compound represented by the formula (I) having an angiotensin II antagonistic activity to be administered at a dose of about 0.01 to 150 mg/patient/day can be administered at a dose of about 0.0002 to 150 mg/patient/day, preferably 0.001 to 60 mg/patient/day, more preferably 0.01 to 20 mg/patient/day by combining with the following daily doses of the following compounds: trichloromethiazide (1 to 8 mg), cyclopenthiazide (0.25 to 1 mg), cyclothiazide (1 to 2 mg), chlorothiazide (500 to 1000 mg), bendroflumethiazide (2 to 10 mg), hydrochlorothiazide (5 to 200 mg), methyclothiazide (2.5 to 5 mg), benzylhydrochlorothiazide (4 to 16 mg), penfluthiazide (1.5 to 7.5 mg), ethiazide (2.5 to 10 mg), hydroflumethiazide (10 to 200 mg), polythiazide (0.25 to 4 mg), meticrane (150 to 300 mg), chlorothalidone (50 to 200 mg), tripamide (15 to 30 mg), **[methrazone]** **metolazone** (2.5 to 5 mg), indapamide (0.5 to 2 mg), quinethazone (25 to 150 mg), clofenamide (50 to 400 mg), furosemide (20 to 500 mg), bumetanide (0.5 to 2 mg), mefruside (1.25 to 50 mg), diltiazem hydrochloride (10 to 200 mg), nicardipine hydrochloride (3 to 40 mg), **[valnidipine]** **barnidipine** hydrochloride (2 to 15 mg),

flunarizine hydrochloride (2 to 10 mg), verapamil hydrochloride (2 to 80 mg), manidipine hydrochloride (2 to 20 mg), cinnarizine (10 to 50 mg), nisoldipine (2 to 10 mg), nitrendipine (2 to 10 mg), nifedipine (3 to 40 mg), nilvadipine (1 to 8 mg), or benidipine (2 to 8 mg). Needless to say, while these dosage ranges can be adjusted by a necessary unit base for dividing a daily dose, as described above, such doses are decided depending on the diseases to be treated, conditions of such diseases, the age, body weight, general health conditions, sex, diet of the patient then treated, dose intervals, administration routes, excretion rate, and combinations of drugs, while taking these and other necessary factors into consideration.

10. I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56, including for continuation-in-in part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

11. I believe that all the errors recited above and being presented for correction in this reissue application arose without any deceptive intention on our part.

Conclusion

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date

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